Claim 26 (Previously presented). Digital storage medium according to Claim **19**, wherein said prediction module comprises a calculation function for calculating the parameters from the lipophilicity and/or the molecular weight of the substance.

Claim 27 (Previously presented). Digital storage medium according to Claim **19**, wherein said calculation function is based on a linear regression of experimentally determined parameter values.

REMARKS/ARGUMENTS

This paper is submitted in response to the non-final official action dated October 31, 2007. Claims 1, 6, 7, 10, 19, and 20 are amended. Reconsideration in view of the Amendment and Arguments presented below is requested.

Claim rejections under 35 USC § 101

The Examiner rejected claims 1-27 because the claimed invention is directed to non-statutory subject matter. He stated that claims 1-9 are drawn to computer "systems" which lack any tangible embodiments. Concerning claims 10-19 he stated that the claims were drawn to methods which would not provide a physical transformation of matter, nor do they provide a concrete, tangible and useful result. Furthermore, concerning claims 19-27 he stated that the claims were drawn to digital storage media which carry out a method which is non-statutory.

Applicants have amended the claims for clarification to recite the practical application of the claimed invention to be a system and method for calculating a pharmacokinetic behavior of a chemical substance in an insect, having an input module for inputting of the physicochemical property of a substance to be studied and for output of simulated concentration/time profiles for a user of said computer system. This amended language finds support on page 4, lines 32-34 of the specification, as well as in Fig. 2.

Applicants submit that claim 1, 10 and claim 19, as amended, now clearly recites a practical application for the present claimed invention thereby overcoming the rejection under 35 U.S.C. §101.

Independent claims 6 and 7 have been similarly amended and thus also have overcome the rejection under 35 U.S.C. §101. The remaining independent claims are dependent from amended claims and therefore overcome the rejection under 35 U.S.C. §101.

Claim rejections under 35 USC § 112, second paragraph

Claims 1-27 are rejected as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.
Applicants have amended the independent claims to clarify the claim language. It appears as if the Examiner had difficulties differentiating the physicochemical properties of the substance to be studied and the substance-dependent parameters, which are calculated from the physicochemical properties of the substance and which are used by the simulation model to simulate the concentration/time profile of the substance in the compartments of an insect - the latter being the result of the simulation.
Accordingly, Claim 1 was amended to clearly differentiate the different parameters used in the simulation. The feature "substance-dependent" was added to the parameter, which is calculated on the basis of the physicochemical property of the substance to be studied. The same amendments were made in Claims 10 and 19.
Additionally in Claim 1 the word "having" was substituted by the word "using" to make clear, that the substance-dependent parameter used by the simulation model is not a priori contained in the simulation model, but is calculated from the physicochemical property of the substance and is used to obtain the concentration/time profile of said substance.

The Examiner stated that in Claim 1 the metes and bounds of the limitation of the modules are unclear. The Examiner further stated that the specification fails to provide a

specific definition of the model. Applicants do not agree with the Examiner. The subject matter of the invention is clearly described. According to the specification and the Figures, the model is described as follows:

The simulation model (102) is a physiologically based pharmacokinetic model of an insect. The simulation model (102) represents the compartments of the insect, and hence makes it possible to predict concentration/time profiles of a chemical substance in the compartments of the insect (page 4, lines 6- 10). The simulation model contains physiological constants (Fig. 1), which depend only on the type of insect to be described (page 4, line 12). To carry out a simulation, at least one substance-dependent parameter has to be provided (page 4, lines 11-15). According to the invention, the substance-dependent parameter is calculated from physicochemical properties of the substance (page 4, lines 25- 31). A concrete example of an embodiment of the simulation model 102 is shown in Fig. 3 - namely a physiological model for a caterpillar. This embodiment of the simulation model is described in detail on pages 6 - 10 of the specification, so that one of ordinary skill in the art is able reproduce it and is able to build up a simulation model of another insect.

Besides the simulation model the claimed computer system includes further modules such as the prediction module, which is also described in the specification. In order to carry out a simulation, at least one substance-dependent parameter has to be provided, which is predicted in the prediction module 110 on the basis of physicochemical properties of the substance (page 4 lines 25 -31). There is an example presented on page 8 lines 26-28 and page 9 lines 1 - 27, where the substance-dependent parameter is the rate coefficient of the inter-compartmental mass transport, which is obtained from the physicochemical properties lipophilicity (described by the distribution coefficient of the substance between water and fat) and the molecular weight. For the prediction of the substance-dependent parameter on the basis of physicochemical properties of the substance in the prediction module 110, according to the invention, a calculation function is used, which is obtained from results of previous experimental studies stored in a databank (page 3 lines 1-6). An example of a calculation function is presented on page 9 lines 14 - 22 and in Fig. 4.

Therefore, applicants submit that the claims are defined by the specification and thus, withdrawal of the outstanding rejections under 35 U.S.C. §112, second paragraph is requested.

Further, the Examiner stated that Claim 6 is unclear, as it is not clearly set forth, where the QSAR model or neural network are to be placed in the system of claim 1. From the specification it is apparent, that the QSAR model or neural network is not necessarily part of the computer system. The physicochemical property, which is the basis for the prediction of the substance-dependent parameter for the simulation, is an input parameter for the simulation model (page 4 lines 32-34). The physicochemical property itself is determined experimentally or from the descriptor of the chemical structure of the substance by means of methods which are known per se, such as QSAR or neural networks (page 2 lines 11-15). Therefore, Claim 6 is amended to include "wherein said physicochemical property is determined from the chemical structure of said chemical substance by means of a QSAR model or a neural network."

Concerning Claim 7, the Examiner stated that the claim is unclear due to how the prediction module is to be "based on" a database. According to the specification (page 4 lines 18- 31) a databank (108) is used for storing a database, which have been obtained on the basis of experimental studies of the pharmacokinetic behavior of test substances in the insect. The database stored in the databank 108 forms the basis of the prediction of the parameter value for a new substance to be studied in the prediction module 110. A calculation rule is obtained from the database, which makes it possible to obtain the substance-dependent parameter from physicochemical properties of the substance. An example of a calculation rule is presented on page 9 lines 14 - 22 and in Fig. 4. Thus, claim 7 was amended to show the interactions of the modules "wherein physicochemical properties of test substances and corresponding substance-dependent parameters determined experimentally for the test substances are stored in a database and are used to obtain a calculation function for prediction of substance-dependent parameters for a new substance to be studied".

Further, according to the Examiner, Claims 10 and 19 are structurally similar in setup to Claim 1 and have similar deficiencies. As already mentioned above, Claims 10 and 19 are amended analogously to Claim 1.

Therefore, applicants submit that the claims are defined by the specification and thus, withdrawal of the outstanding rejections under 35 U.S.C. §112, second paragraph is requested.

Claim rejections under 35 USC § 102

Claims 1-27 are rejected as being anticipated by Keane. Applicants respectfully disagree with the Examiner. Anticipation requires identity of invention. *See* MPEP 2131. *See also Glaverbel Societe Anonyme v. Northlake Mktg. & Supply*, 33 USPQ2d 1496, 1498 (Fed. Cir. 1995). Each and every element recited in a claim must be found in a single prior art reference and arranged as in the claims. *In re Marshall*, 198 USPQ 344, 346 (CCPA 1978); *Lindemann Maschinenfabrik GMBH v. American Hoist and Derrick Co.*, 221 USPQ 481, 485 (Fed. Cir. 1984). There must be no differences between what is claimed and what is disclosed in the prior art reference. *In re Kalm*, 154 USPQ 10, 12 (CCPA 1967.) Moreover, it is incumbent upon the Examiner to identify wherein each and every facet of the claimed invention is disclosed in the applied reference. *Ex parte Levy*, 17 USPQ2d 1461, 1462 (BPAI 1990).

Keane disclosed an approach for analyzing bio-transport dynamics by applying finite-element techniques with first principles and empirical relationships to a bio-transport system [0016]. The bio-transport system therefore is mainly a fluid flow model, which provides sophisticated bio-transport dynamic data as a function of time and of the spatial position locating each element defined.

Hence, the subject matter of Keane is totally different from the subject matter of the present invention being a computer system for calculating a pharmacokinetic behavior of a chemical substance in an insect on the basis of the physicochemical properties of said substance (Claim 1). Therefore one of ordinary skill in the art would not consider the

disclosure of Keane, when searching for a tool to predict the pharmacokinetic behavior of a chemical substance in an insect.

But even if one would take into account the disclosure of Keane, the simulation tool of Keane is not appropriate to provide the results of the subject matter of the present invention. According to paragraph [0051] the method of Keane may be practiced to simulate the transport of fluids, energy, materials, chemicals and biologicals in any bio-transport system - including insects. According to paragraphs [0268] and the following paragraphs, which were referenced to by the Examiner, organs can be included in the simulation of a biotransport system as well.

Thus, Keane teaches that the disclosed simulation tool can be adapted to insects, although all examples were related to the human circulatory system. However, it has to be noted that a physiological model of an insect with respect to the relevant transport processes is fundamentally different from a physiological model of a mammalian (see Fig 3 of the present invention). The mammalian organism exhibits a closed-loop blood system. The mass transport between different compartments of the mammalian organism occurs via the blood stream. By contrast the organism of an insect is built up differently: the haemolymph, which has similar functions like blood in a mammalian organism, is pumped over by an open tube-shaped heart. The organs float within the haemolymph and are in direct contact with the haemolymph. The inter-compartmental mass transport in an insect does not occur via a directed transport system but via indirect transport (diffusion). Therefore the parameterization of the differential equations, which balance the mass transport between the different compartments of an organism, is different for an insect and is a problem, which has to be solved. Besides physiological parameters such as volumes of organs which are published in literature a couple of parameters such as distribution and transport coefficients have to be provided, which depend on the chemical substance to be studied.

Therefore it is a non trivial task to simulate the pharmacokinetic behavior of a chemical-

substance in an insect. Keane claims that the disclosed simulation tool can be adapted to insects, but there is no indication, how the organism of the insect should be represented within the model. There is no indication, how to find the parameters for the differential equations for the mass transport between the compartments of the organism. So we doubt that the simulation model disclosed by Keane can be adapted to insects.

Furthermore the simulation model of Keane lacks important features, which are fundamental aspects of the subject matter of the present invention. Keane neither discloses nor suggests the use of a prediction module for predicting at least one substance-dependent parameter, which has to be provided to carry out the simulation, on the basis of a physicochemical property of a substance to be studied.

Keane does not anticipate the current invention in which the simulation model is based on at least one substance-dependent parameter, which is predicted from physicochemical properties of the substance to be studied.

Accordingly, the rejection of claims 1-27 under 35 U.S.C. 102 as being anticipated by Keane should therefore be withdrawn.

CONDITIONAL PETITION FOR EXTENSION OF TIME

If entry and consideration of the amendments above requires an extension of time, Applicants respectfully request that this be considered a petition therefore. The Assistant Commissioner is authorized to charge any fee(s) due in this connection to Deposit Account No. 14-1263.

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ADDITIONAL FEE

Please charge any insufficiency of fees, or credit any excess, to Deposit Account No. 14-1263.

Respectfully submitted,
NORRIS McLAUGHLIN & MARCUS, P.A.

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